

*By D. A. Shultz 5*

IONIC MOLECULAR CONJUGATES  
OF BIODEGRADABLE POLYESTERS AND BIOACTIVE POLYPEPTIDES

Cross Reference To Related Applications

This application is a continuation-in-part of copending Application No. 08/867,308, filed June 2, 1997, which will issue as U.S. Patent No. 5,863,985 on January 26, 1999, which is a continuation application of Application No. 08/464,735, filed June 29, 1995, now issued as 5,672,659 on September 30, 1997, which is a National Phase application of PCT/US94/00148, filed January 5, 1994, which is a PCT Phase application of Irish Application No. 930005 filed January 6, 1993.

Background of the Invention

This invention pertains to sustained release of bioactive polypeptides.

Many drug delivery systems have been developed, tested and utilized for the controlled *in vivo* release of pharmaceutical compositions. For example, 15 polyesters such as poly (DL-lactic acid), poly (glycolic acid), poly ( $\epsilon$ -caprolactone) and various other copolymers have been used to release biologically active molecules such as progesterone; these have been in the form of microcapsules, films, or rods (Pitt CG, Marks, TA, and Schindler, A. 1980). Upon implantation of 20 the polymer/therapeutic agent composition, for example subcutaneously or intramuscularly, the therapeutic agent is released over a specific period of time. Such biocompatible biodegradable polymeric systems are designed to permit the entrapped therapeutic agent to diffuse from the polymer matrix. Upon release of the therapeutic agent, the polymer is degraded *in vivo*, obviating surgical removal 25 of the implant. Although the factors that contribute to polymer degradation are not well understood, it is believed that such degradation for polyesters may be regulated by the accessibility of ester linkages to non-enzymatic autocatalytic hydrolysis of the polymeric components.

Several EPO publications and US Patents have addressed issues of 30 polymer matrix design and its role in regulating the rate and extent of release of therapeutic agents *in vivo*.

For example, Deluca (EPO Publication 0 467 389 A2/Univ of Kentucky)

**This application is a 371 of PCT/US00/01753 filed 01/26/2000,  
which is a continuation of serial number 09/237,405 filed 01/26/1999  
now patent number 6,221,958**